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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,650	02/19/2002	Katsumi Fujimoto	14875-101001/C1-107PCT-US	7203

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/078,650	**Applicant(s)** FUJIMOTO ET AL.	
	Examiner Jennifer Dunston	**Art Unit** 1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 June 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *04 April 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following ~~rejection(s)~~: objection to claims 2-4.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-6,9,10 and 15-19*.
   Claim(s) withdrawn from consideration: *8*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See continuation sheet.
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). 6/1/2006
13. ☐ Other: _____.

CONTINUATION SHEET

Applicant's arguments, see page 5 of 11, filed 6/1/2006, with respect to the objection of claims 2-4 have been fully considered and are persuasive. The previous objection of claims 2-4 has been withdrawn.

Claims 1-6, 9-10, and 15-19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. This rejection is maintained for reasons of record set forth in the papers mailed 1/3/05, and 10/5/2005. Applicants' arguments filed 6/1/2006 have been fully considered but they are not deemed to be persuasive.

The response asserts that the claimed DEC2 nucleic acids have significant homology to members of the DEC1 subfamily, including DEC1 and SHARP-1, and thus the claimed nucleic acids have utility in controlling cell development and differentiation, as markers of development and differentiation, and as targets in the development of pharmaceutical agents for disorders, such as osteoarthritis, associated with the proteins of the present invention. This assertion is not found to be persuasive for reasons of record set for on pages 11-12 of the Office action mailed 10/5/2005. Further, the response asserts that the specification describes DEC2 as important in elucidating the differentiation and deformation mechanisms of cartilage and is therefore expected to be useful in developing therapies for the treatment of osteoarthritis, rheumatoid arthritis, etc. The response points to page 5, lines 7-22, for support of this assertion. This assertion appears to be based upon the similarity between the claimed polynucleotides and the sequence of DEC1. At page 2 of the instant specification, DEC1 is described as being induced by dibutyryl cAMP in chondrocytes and as being expressed in chondrocytes. At page 5, lines 7-22, the specification

indicates that DEC2 shares greater homology with SHARP than DEC1. In contrast to DEC1, SHARP is induced by the addition of NGF to PC12 cells or by the addition of kainic acid *in vivo* and is thought to be involved in the plasticity of cells of the central nervous system in rats (page 2 and page 5, lines 7-22). Thus, the assertion that DEC2 is involved in the differentiation and deformation mechanisms of cartilage is merely a hypothesis set forth in the specification, which can be challenged by a second hypothesis that DEC2 functions in the plasticity of the central nervous system. However, to determine the actual function of DEC2 one would have to conduct further experimentation. Thus, this argument does not provide evidence of a specific and substantial utility for the claimed nucleic acids.

The response assets that the DEC1 subfamily of bHLH transcription factors, which comprises DEC1, Stra13, and SHARP-1 all, has well-established utilities as regulators of differentiation. Further the response asserts that the DEC2 proteins share 90% or greater identity with the DEC1 and SHARP-1 proteins in the conserved bHLH region (i.e., the region that dictates activity, e.g., regulation of differentiation). While it is credible that the claimed polynucleotides encode proteins involved in differentiation, the other two prongs of the utility test are not satisfied. This is a general utility for bHLH proteins. The specific functions and properties of the bHLH proteins differ in spite of the high degree of sequence identity between the related members of the DEC1 subfamily. As stated on page 2 of the instant specification, human DEC1 is upregulated by dibutyryl cAMP in chondrocytes, mouse Stra13 is induced in embryonal carcinoma cells by retinoic acid, and rat SHARP is induced by the addition of NGF to PC12 cells and by the addition of kainic acid *in vivo*. The specification does not indicate that all members of the DEC1 subfamily have a common function. Thus, one can classify the DEC2

protein within the DEC1 subfamily; however, one cannot assign a specific function to the DEC2 protein without conducting significant further experimentation to confirm a real world context of use in modulating cartilage or neural development, for example. Moreover, the diverse functions recited in the specification are objective evidence that one would not know the function of the claimed proteins without conducting significant further experimentation.

The response asserts that the Examiner did not address all utilities asserted in the specification. The asserted unaddressed utilities are (i) "The present invention provides novel bHLH type transcription factors and DNA encoding the proteins," and (ii) "For example, 'DEC2' is important in elucidating the differentiation and deformation mechanisms of cartilages..." The first asserted utility is not specific or substantial. As addressed on page 5 of the Office action mailed 10/5/2005, there is no well established utility for the nucleic acid and encoded proteins because the nucleic acids and proteins are not completely described in the prior art and there is no specific function taught which is similar enough to a prior art nucleic acid or protein so as to support a well established utility. At pages 5-7 of that action, the Examiner indicates that the specification does not teach the function of the claimed nucleic acid or encoded protein, and thus the claimed nucleic acids do not have a specific and substantial utility. Regarding the assertion that DEC2 is important in elucidating the differentiation and deformation mechanisms of cartilages, the Examiner addressed this utility under item 1 listed on page 5 of the Office action mailed 10/5/2005. The specification does not teach the function of DEC2 in cartilage differentiation or deformation, and thus this is not a specific and substantial utility.

The response argues that the asserted utilities are specific and not a general utility that would be applicable to the broad class of the invention. This is not found persuasive because the

asserted utilities are those based on the functions of the broad class of DEC1 subfamily bHLH proteins and are not based upon the specific function of DEC2 in a particular cell type and differentiation state. The fact that the broad classes of ligases have different substrate specificity is not found persuasive in light of the different disclosed functions for DEC1 subfamily bHLH proteins and the unknown function of the proteins encoded by the claimed nucleic acids. Further, the response asserts that more is known about the claimed polynucleotides than was known about the ESTs at issue in *Fisher*. However, the identification of the claimed polynucleotides as encoding a bHLH factor only indicates that the protein is capable of binding DNA and does not provide the specific genes regulated by the transcription factor. The polypeptides may regulate any of a number of genes or developmental pathways, and the specification does not identify those genes or pathways with certainty.

The response argues that the asserted utilities are substantial. The response asserts that the claimed nucleic acids are "likely to play a role" in the differentiation of cartilage; thus, the specific tissue type in which the proteins function is identified. This is not found persuasive, as there is no evidence of record that teaches that DEC2 is specifically expressed in cartilage in manner relevant to osteoarthritis. To confirm this assertion, one would be required to perform significant further studies. Utilities that require carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. Further, the response asserts that the protein can be used in screening substances to be used to treat osteoarthritis. Even if the protein were expressed in chondrocytes, further research would need to be conducted to determine whether the protein plays a significant role in the pathogenesis of osteoarthritis. The mere presence of a protein does not guarantee that it plays a role in a

particular disease. Again, one would be required to carry out further research, which indicates that this is not a substantial utility.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

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PRIMARY EXAMINER